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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/525,955	03/31/2006	Bernd Rehm	3652-50	3076

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EXAMINER	
MEAH, MOHAMMAD Y	

ART UNIT	PAPER NUMBER
1652	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/525,955

Applicant(s)

REHM, BERND

Examiner

Mohammad Meah

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 31 August 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 30-99 is/are pending in the application.
- 4a) Of the above claim(s) 30-58, 61-71 and 96-98 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 59, 60, 72-95 and 99 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>See Continuation Sheet</u> . | 6) <input type="checkbox"/> Other: _____ |

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :2/28/05, 4/5/05, 10/13/06, 10/31/06.

DETAILED ACTION

Applicants' election without traverse of group 25 (claims 59-60, 72-95) in their response of 08/31/2007 is acknowledged.

Election/Restriction

Applicant, on date 08/31/2007, elected without traverse group 25 (claims 59-60, 72-95) drawn to method of producing polymer surface bound protein using host cell expressed with polymer synthase. Groups 1-24 and 26-37 (claims 30-58 and 61-71 and 96-98) of election/restriction-office action of date 7/2 /2007 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected Groups. Applicant argument for inclusion of claim 99 to the restriction requirement is considered. Claim 99 will be included in elected group 25.

Priority

Acknowledgement is made of applicant's application priority date of 8/22/2003 based on PCT/DE03/02799.

Claim Objections

Claim 60 is objected to contain non-elected subject matter (polymer size determining protein, PhA thiolase etc) . Appropriate correction is required.

Claims 59-60, 72-95 and 99 is objected to contain non elected subject matters (polymer particle forming proteins that are not elected subject matter (polymer synthase))

Claim Rejections

35 U.S.C 112

35 U.S.C. 112 2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 59-60, 72-95 and 99 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 60- The protein involved in the formation of polymer particles"- is confusing as no such protein defined in the part of claim 59.

Claims 59 and 99 the recitation "biologically active" makes the claim indefinite and vague. As it is unclear what "biologically active" term means and what are these derivatives from.

35 U.S.C. 112 1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most

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nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 59-60, 72-95 and 99 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 59-60, 72-95 and 99 are directed to a method of producing any polymer conjugates comprising any polymeric compound conjugated with any protein or any biologically active substance (any bioactive organic compound or protein) using any host cell expressed with any polymer synthase from any source. The specification fails to describe how any polymer conjugates comprising any polymeric compound conjugated with any protein or any biologically active substance (any bioactive organic compound or protein) using any host cell expressed with any polymer synthase. The specification fails to describe in any fashion the physical (structure) and/or chemical properties of the claimed class of polymer particles, protein and biomolecules and their biological function. A biomolecule can be any molecule i.e., antibody, protein, enzyme, hormone, DNA, RNA, lectin, glycoprotein, bioactive small organic compounds, etc. Similarly, the specification fails to describe the structure of all polymer particles, biomolecules and protein. Conjugation of a polymer compound to a protein or biomolecule depends on the nature of functional groups in those molecules that are to be conjugated. No relationship between the structure of all polymer compounds, and proteins is given in the specification. Moreover specification does not describe how any host cell can be used to make any polymer conjugates comprising any polymeric compound conjugated with any protein or

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any biologically active substance (any bioactive organic compound or protein). Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Claims 59-60, 72-95 and 99 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for producing any polymer conjugates comprising R-hydroxy butyric acid polymer compound conjugated with FLAG –PhaC1 fusion protein using *E. coli* expressed with plasmid pBBad-P containing *R. eutropha* polymer synthase, does not reasonably provide enablement for method of producing any polymer conjugates comprising any polymeric compound conjugated with any protein or any biologically active substance (any bioactive organic compound or protein) using any host cell expressed with any polymer synthase from any source. The specification fails to describe how any polymer conjugates comprising any polymeric compound conjugated with any protein or any biologically active substance (any bioactive organic compound or protein) can be made using any host cell expressed with any polymer synthase from any source. The specification fails to describe in any fashion the physical and/or chemical properties of polymer conjugate compounds as well as conjugatable protein and bioactive compound. The physical and/or chemical properties of the compounds that are conjugated and the physical and/or chemical properties of the protein is important for conjugation and also nature of polymer synthase as well as host cell used for the preparation of the compound.. As the physical and/or chemical properties of the polymer compounds that are conjugated and the physical and/or chemical properties of the bioactive compound and the protein are not known and also not known the structure of polymer synthase,

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one of ordinary skill in the art would not be able to make and use all such substances without undue experimentation to first find what substances in fact fall within the claimed class.

Furthermore, the claimed compounds are likely to include many compounds, which one of ordinary skill in the art would be unable to make and use without undue experimentation, even if it was known or expected that the substance be within the scope of the claims.

Factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands* (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 59-60, 72-95 and 99 are so broad as to encompass method of producing any polymer conjugates comprising any polymeric compound conjugated with any protein or any biologically active substance (any bioactive organic compound or protein) using any host cell expressed with any polymer synthase. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to any method of producing any polymer conjugates comprising any polymeric compound conjugated with any protein or any biologically active substance (any bioactive organic compound or protein) using any host cell expressed with any polymer synthase. In view of the great breaths of claims 59-60, 72-95 and 99 , amount of experimentation required to make broad class of polymer conjugates comprising any polymeric compound conjugated with any protein or any biologically active substance (any

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bioactive organic compound or protein) using any host cell expressed with any polymer synthase and, the lack of guidance, working examples, unpredictability of the art in predicting the function (polymer synthase activity) from protein's structure (Whisstock, et al. Quarterly Rev. Biophy. 2003, 36, pp 307-340), the claimed invention would require undue experimentation. As such the specification fail to teach one of ordinary skill how to use the full scope of the claims.

Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to precipitation of silica by a few polymer synthase polypeptides

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass method of producing any polymer conjugates comprising any polymeric compound conjugated

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with any protein or any biologically active substance (any bioactive organic compound or protein) using any host cell expressed with any polymer synthase, because the specification does **not** establish: (A) regions of the protein structure which may be modified to make polymer particles (B) the general tolerance of modification and extent of such tolerance on polymer synthase activity; (C) a rational and predictable scheme for modifying any polymer synthase polypeptide amino acid residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including method of producing any polymer conjugates comprising any polymeric compound conjugated with any protein or any biologically active substance (any bioactive organic compound or protein) using any host cell expressed with any polymer synthase. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of oxidoreductase variants, having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir,1988).

CLAIM Rejection - 35 U.S.C 103a

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 59-60, 72-95 and 99 are rejected under 35 U.S.C. 103(a) by Madison et al. (Microbiol Mol Biol rev 1999 vol.63, pp 21-53, from IDS) or Pieper-furst et al (US 6022729, from IDS).

Madison et al. disclose processes for preparing polymeric particles from polyhydroxyalkanoates (PHAs) synthesized *inter alia* in *Ralstonia eutropha* and *Escherichia coli* (pages 37 and 42) using genes from the PHA biosynthetic pathway (pages 26-29), wherein fatty acids and other hydrocarbons (including those with functional side groups) may be used as substrates (pages 30-33). Further, they disclose that particle size is determined by the amount of particle-binding proteins present, including phasins (phaP) and PHA synthase, since phasin overexpression leads to an increased number of small particles, and that the molecular weight of the polymer is determined by the ratio of substrate to enzyme.

Pieper-furst et al disclose method of producing PHA particles surface bound to the lipids and proteins and other proteins, comprising a particle binding domain (columns 4, 12 and 19). A person skilled in the art is motivated to immobilize a bioactive

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substance (protein or other biomolecule conjugated via coupling reagent or coupling functional group) in order to easy transport said substance bound to the surface of the polymer particle.

As such it would have been obvious to one of ordinary skill in the art to use processes for preparing polymeric particles from polyhydroxyalkanoates (PHAs) synthesized *inter alia* in *Ralstonia eutropha* and *Escherichia coli* (pages 37 and 42) using genes from the PHA biosynthetic pathway (pages 26-29) as taught by Madison et al. and use the resulting polymer particle in the method of producing PHA particles surface bound to the lipids and proteins and other proteins, comprising a particle binding domain (columns 4, 12 and 19) in order to easy transport said substance bound to the surface of the polymer particle as taught by Pieper-furst et al.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mohammad Meah whose telephone number is 571-272-1261. The examiner can normally be reached on 8:30-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


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Examiner, Art Unit 1652

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